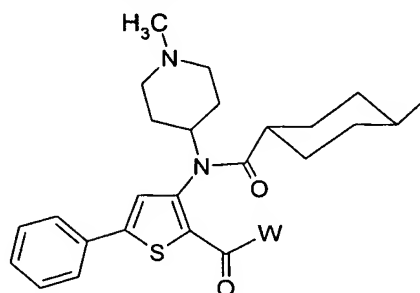


This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended): A compound represented by formula I:

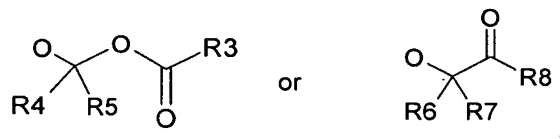


(I)

or a pharmaceutically acceptable salt thereof;

wherein [[:]]

W is C₁₋₁₂ alkyloxy, C₆₋₁₂ arylalkyloxy, amino acid ester, nucleoside, C₆₋₁₂ heteroarylalkyloxy, C₆ aryloxy, 5-6 membered heteroarylalkyloxy,



R₃ and R₈ are each independently C₁₋₁₂ alkyl, C₆₋₁₀ aryl, C₆₋₁₀ arylalkyl, C₃₋₁₀ heterocycle, C₃₋₁₂ heteroarylalkyl, C₆₋₁₂ aralkyl, C₁₋₁₂ alkyloxy, C₆₋₁₀ aryloxy or NR₁₀R₁₁;

R₁₀ and R₁₁ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₂ aryl, C₃₋₁₀ heterocycle, C₆₋₁₂ aralkyl or C₃₋₁₀ heteroarylalkyl;

R₄ and R₅ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₀ aryl, -O(CO)C₁₋₆ alkyl or C₃₋₁₀ heterocycle; and

R₆ and R₇ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₀ aryl, -O(CO)C₁₋₆ alkyl or C₃₋₁₀ heterocycle;

wherein

the above alkyl groups are each a straight chain or branched chain hydrocarbon moiety which optionally contain at least one unsaturated group and which is optionally substituted by one or more of halogen, nitro, nitroso, SO₃C₁₋₆ alkyl, SO₂C₁₋₆ alkyl, PO₃RcRd, amido, C₁₋₆ alkyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, amino, COOH, C(O)O-C₁₋₆ alkyl, cyano, azido, amidino or guanido;

Rc and Rd are each independently H or C₁₋₆ alkyl or Rc and Rd are taken together with the oxygen atoms to form a 5 to 10 membered heterocycle;

the above cycloalkyl groups are each a cyclic alkyl which optionally contain at least one unsaturated group;

the above alkyloxy are each an alkyl group as defined above which is covalently bonded to the adjacent atom through an oxygen atom;

the above amino groups are each optionally substituted by alkyl, aryl, or arylalkyl;

the above amido groups are each -CONH₂, CONH(isopropyl), CON(CH₃)₂;

the above aryl groups are each a carbocyclic moiety containing at least one benzenoid-type ring which is optionally substituted by one or more of halogen, nitro, nitroso, SO₃C₁₋₆ alkyl, SO₂C₁₋₆ alkyl, PO₃RcRd, amido, C₁₋₆ alkyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, amino, COOH, C(O)O-C₁₋₆ alkyl, cyano, azido, amidino or guanido;

the above aralkyl are each an aryl group attached to the adjacent atom by a C₁₋₆ alkyl, C₁₋₆ alkenyl, or C₁₋₆ alkynyl;

the above aralkyloxy groups are each an aralkyl group which is covalently bonded to the adjacent atom through an oxygen atom;

the above amino acid ester groups are each an essential or non-essential alpha amino acid, beta amino acid or esterified amino acid carboxylate;

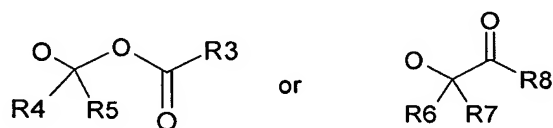
the above heterocycle groups are each a saturated or unsaturated, cyclic moiety wherein

VIRO-6

said cyclic moiety is interrupted by at least one heteroatom, selected from oxygen, sulfur and nitrogen, which is optionally substituted by halogen, nitro, nitroso, $\text{SO}_3\text{C}_{1-6}$ alkyl, $\text{SO}_2\text{C}_{1-6}$ alkyl, PO_3RcRd , amido, C_{1-6} alkyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{6-12} aryloxy, $\text{C}(\text{O})\text{C}_{1-6}$ alkyl, $\text{C}(\text{O})\text{C}_{6-12}$ aryl, $\text{C}(\text{O})\text{C}_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, amino, COOH , $\text{C}(\text{O})\text{O}-\text{C}_{1-6}$ alkyl, cyano, azido, amidino or guanido; and

the above heteroaralkyl groups are each a heterocycle group attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl.

2. (Previously Presented): A compound of claim 1, wherein W is C_{1-12} alkyloxy, amino acid ester,



3. (Previously Presented): A compound of claim 1, wherein, R_3 and R_8 are each independently C_{1-12} alkyl, C_{6-10} aryl, C_{6-10} arylalkyl, C_{3-10} heterocycle, C_{3-12} heteroaralkyl, C_{6-12} aralkyl, C_{1-12} alkyloxy, C_{6-10} aryloxy or $\text{NR}_{10}\text{R}_{11}$; and

R_{10} and R_{11} are each independently H, C_{1-12} alkyl, C_{6-12} aryl, C_{3-10} heterocycle, C_{6-12} aralkyl or C_{3-10} heteroaralkyl.

4. (Previously Presented): A compound of claim 1, wherein R_4 and R_5 are each independently H, C_{1-12} alkyl, C_{6-10} aryl, $-\text{O}(\text{CO})\text{C}_{1-6}$ alkyl or C_{3-10} heterocycle.

5. (Previously Presented): A compound of claim 1, wherein R_4 and R_5 together to form a 3-6 membered cycloalkyl.

6. (Previously Presented): A compound of claim 1, wherein R_6 and R_7 are each independently H, C_{1-12} alkyl, C_{6-10} aryl, $-\text{O}(\text{CO})\text{C}_{1-6}$ alkyl or C_{3-10} heterocycle.

7. (Previously Presented): A compound of claim 1, wherein R₆ and R₇ together form a 3-6 membered cycloalkyl.

8. (Previously Presented): A compound of claim 1, wherein R₁₀ and R₁₁ are each independently H, C₁₋₁₂ alkyl, or C₃₋₁₀ heterocycle.

9. (Currently Amended): A compound selected from:

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2,2-DIMETHYL-PROPIONYLOXYMETHYL;

4-[(2-ISOPROPOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

4-[(2-ISOPROPYLCARBAMOYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-{(4-METHYL-CYCLOHEXANECARBONYL)-[2-(5-METHYL-2-OXO-[1,3]DIOXOL-4-YLMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-AMINO}-PIPERIDINIUM;

4-[[2-(1-ISOPROPOXYCARBONYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-[1-(2,2-DIMETHYL-PROPIONYLOXY)-ETHOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(ISOPROPOXYCARBONYLOXY-PHENYL-METHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-CYCLOHEXYLOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-

VIRO-6

THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[{2-[(2,2-DIMETHYL-PROPIONYLOXY)-PHENYL-METHOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL}-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(5-PHENYL-2-PROPIONYLOXYMETHOXYCARBONYL-THIOPHEN-3-YL)-AMINO]-PIPERIDINIUM; CHLORIDE;

4-[[2-(FURAN-2-CARBONYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-BENZOYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-CYCLOHEXANECARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(5-PHENYL-2-SUCCINYL-17(3-TERT-BUTOXYCARBONYLMETHYL-CARBAMOYL)-METHYL-PROPYL)-7,12-DIHYDROXY-10,13-DIMETHYL-HEXADECAHYDRO-CYCLOPENTA(A)PHENANTHREN-3-YLOYMETHOXYCARBONYL-THIOPHEN-3-YL)AMINO]-PIPERIDINIUM CHLORIDE;

METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(5-PHENYL-2-SUCCINYL-17(3-CARBONYLMETHYL-CARBAMOYL)-METHYL-PROPYL)-7,12-DIHYDROXY-10,13-DIMETHYL-HEXADECAHYDRO-CYCLOPENTA(A)PHENANTHREN-3-YLOYMETHOXYCARBONYL-THIOPHEN-3-YL)AMINO]-PIPERIDINIUM CHLORIDE;

4-[(2-ETHOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(2-

VIRO-6

PHENOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-AMINO]-PIPERIDINIUM CHLORIDE;

1-METHYL-4-{(4-METHYL-CYCLOHEXANECARBONYL)-[2-(MORPHOLINE-4-CARBONYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-AMINO}-PIPERIDINIUM CHLORIDE;

4-[[2-[1-(2,2-DIMETHYL-PROPIONYLOXY)-2-METHYL-PROPOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-SEC-BUTOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(1-ISOPROPOXYCARBONYLOXY-2-METHYL-PROPOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-SEC-BUTOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID TERT-BUTOXYCARBONYLAMINOACETOXYMETHYL ESTER;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2-TERT-BUTOXYCARBONYLAMINO-3-METHYL-BUTYRYLOXYMETHYL ESTER;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID AMINOACETOXYMETHYL ESTER, BIS TRIFLUOROACETATE SALT;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2-AMINO-3-METHYL-BUTYRYLOXYMETHYL ESTER, BIS TRIFLUOROACETATE SALT;

VIRO-6

4-[[2-(1-ISOPROPOXYCARBONYLOXY-1-METHYL-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 1-(1-METHYL-CYCLOHEXANECARBONYLOXY)-ETHYL ESTER;

4-[[2-(1-TERT-BUTOXYCARBONYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-((4-METHYL-CYCLOHEXANECARBONYL)-{2-[1-(1-METHYL-CYCLOHEXANECARBONYLOXY)-ETHOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL}-AMINO)-PIPERIDINIUM;

PYRROLIDINE-1,2-DICARBOXYLIC ACID 1-TERT-BUTYL ESTER 2-{3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBONYLOXYMETHYL} ESTER;

4-METHYL-PIPERAZINE-1-CARBOXYLIC ACID 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBONYLOXYMETHYL ESTER DIHYDROCHLORIDE SALT;

~~4-Methyl-piperazine-1-carboxylic acid 3-[(4-methyl-cyclohexanecarbonyl)-(1-methyl-piperidin-4-yl)-amino]-5-phenyl-thiophene-2-carbonyloxymethyl ester dihydrochloride salt;~~

4-[[2-(1-CYCLOHEXYLOXYCARBONYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

2-{3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBONYLOXYMETHOXYCARBONYL}-PYRROLIDINIUM; BIS-TRIFLUORO-ACETATE;

4-[[2-(1-ISOBUTYRYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

VIRO-6

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID PYRIDIN-2-YL ESTER;

4-[[2-(1-ACETOXY-1-METHYL-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2-OXO-PYRROLIDIN-1-YLMETHYL ESTER;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(2-PHENOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-AMINO]-PIPERIDINIUM CHLORIDE;

1-METHYL-4-{(4-METHYL-CYCLOHEXANECARBONYL)-[5-PHENYL-2-(PYRIDIN-3-YLOXYCARBONYL)-THIOPHEN-3-YL]-AMINO}-PIPERIDINIUM; CHLORIDE;

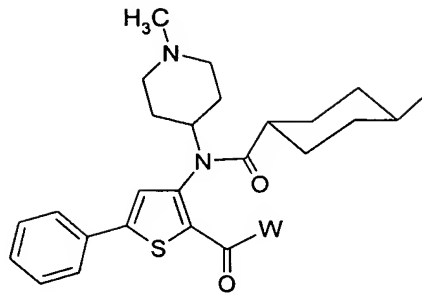
4-{{2-[1-(4-HYDROXY-5-HYDROXYMETHYL-TETRAHYDRO-FURAN-2-YL)-2-OXO-1,2-DIHYDRO-PYRIMIDIN-4-YLCARBAMOYL]-5-PHENYL-THIOPHEN-3-YL}-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(1-METHOXYCARBONYL-2-METHYL-PROPYLCARBAMOYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(1-METHOXYCARBONYL-ETHYLCARBAMOYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM;

and pharmaceutically acceptable salts thereof.

10. (Currently Amended): A method for treating or preventing a Flaviviridae viral infection in a host comprising administering to the host a therapeutically effective amount of at least one compound of formula I:

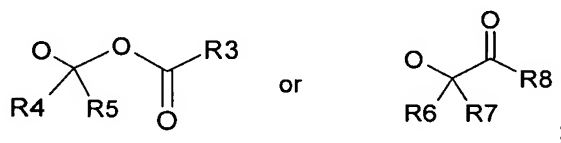


(I)

or a pharmaceutically acceptable salt thereof;

wherein [[:]]

W is C₁₋₁₂ alkyloxy, C₆₋₁₂ arylalkyloxy, amino acid ester, nucleoside, C₆₋₁₂ heteroarylalkyloxy, C₆ aryloxy, 5-6 membered heteroaryloxy,



R₃ and R₈ are each independently C₁₋₁₂ alkyl, C₆₋₁₀ aryl, C₆₋₁₀ arylalkyl, C₃₋₁₀ heterocycle, C₃₋₁₂ heteroarylalkyl, C₆₋₁₂ aralkyl, C₁₋₁₂ alkyloxy, C₆₋₁₀ aryloxy or NR₁₀R₁₁;

R₁₀ and R₁₁ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₂ aryl, C₃₋₁₀ heterocycle, C₆₋₁₂ aralkyl or C₃₋₁₀ heteroarylalkyl;

R₄ and R₅ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₀ aryl, -O(CO)C₁₋₆ alkyl or C₃₋₁₀ heterocycle; and

R₆ and R₇ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₀ aryl, -O(CO)C₁₋₆ alkyl or C₃₋₁₀ heterocycle;

wherein

the above alkyl groups are each a straight chain or branched chain hydrocarbon moiety which optionally contain at least one unsaturated group and which is optionally substituted by one or more of halogen, nitro, nitroso, SO₃C₁₋₆ alkyl, SO₂C₁₋₆ alkyl, PO₃RcRd, amido, C₁₋₆ alkyl,

VIRO-6

C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, amino, COOH, C(O)O-C₁₋₆ alkyl, cyano, azido, amidino or guanido;

Rc and Rd are each independently H or C₁₋₆ alkyl or Rc and Rd are taken together with the oxygen atoms to form a 5 to 10 membered heterocycle;

the above cycloalkyl groups are each a cyclic alkyl which optionally contain at least one unsaturated group;

the above alkyloxy are each an alkyl group as defined above which is covalently bonded to the adjacent atom through an oxygen atom;

the above amino groups are each optionally substituted by alkyl, aryl, or arylalkyl;

the above amido groups are each -CONH₂, CONH(isopropyl), CON(CH₃)₂;

the above aryl groups are each a carbocyclic moiety containing at least one benzenoid-type ring which is optionally substituted by one or more of halogen, nitro, nitroso, SO₃C₁₋₆ alkyl, SO₂C₁₋₆ alkyl, PO₃RcRd, amido, C₁₋₆ alkyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, amino, COOH, C(O)O-C₁₋₆ alkyl, cyano, azido, amidino or guanido;

the above aralkyl are each an aryl group attached to the adjacent atom by a C₁₋₆ alkyl, C₁₋₆ alkenyl, or C₁₋₆ alkynyl;

the above aralkyloxy groups are each an aralkyl group which is covalently bonded to the adjacent atom through an oxygen atom;

the above amino acid ester groups are each an essential or non-essential alpha amino acid, beta amino acid or esterified amino acid carboxylate;

the above heterocycle groups are each a saturated or unsaturated, cyclic moiety wherein said cyclic moiety is interrupted by at least one heteroatom, selected from oxygen, sulfur and nitrogen, which is optionally substituted by halogen, nitro, nitroso, SO₃C₁₋₆ alkyl, SO₂C₁₋₆ alkyl, PO₃RcRd, amido, C₁₋₆ alkyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, amino, COOH, C(O)O-C₁₋₆ alkyl, cyano, azido, amidino or guanido; and

the above heteroaralkyl groups are each a heterocycle group attached to the adjacent atom by a C₁₋₆ alkyl, C₁₋₆ alkenyl, or C₁₋₆ alkynyl.

11. (Previously Presented): A method of claim 10, further comprising administering at least one additional agent which is a viral serine protease inhibitor, viral polymerase inhibitor, viral helicase inhibitor, immunomodulating agent, antioxidant agent, antibacterial agent, therapeutic vaccine, hepatoprotectant agent or antisense agent.

12. (Previously Presented): A method of claim 11, wherein the additional agent is interferon α , ribavirin, silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine or cyclosporin.

13. (Previously Presented): A method according to claim 10, wherein the Flaviviridea viral infection is hepatitis C viral infection (HCV).

14. (Currently Amended): A method for treating or preventing a Flaviviridae viral infection in a host comprising administering to the host a therapeutically effective amount of at least one compound selected from:

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2,2-DIMETHYL-PROPIONYLOXYMETHYL;

4-[(2-ISOPROPOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

4-[(2-ISOPROPYLCARBAMOYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-{(4-METHYL-CYCLOHEXANECARBONYL)-[2-(5-METHYL-2-OXO-[1,3]DIOXOL-4-YLMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-AMINO}-

VIRO-6

PIPERIDINIUM;

4-[[2-(1-ISOPROPOXYCARBONYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[{2-[1-(2,2-DIMETHYL-PROPIONYLOXY)-ETHOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL}-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(ISOPROPOXYCARBONYLOXY-PHENYL-METHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-CYCLOHEXYLOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[{2-[(2,2-DIMETHYL-PROPIONYLOXY)-PHENYL-METHOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL}-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(5-PHENYL-2-PROPIONYLOXYMETHOXYCARBONYL-THIOPHEN-3-YL)-AMINO]-PIPERIDINIUM CHLORIDE;

4-[[2-(FURAN-2-CARBONYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-BENZOYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-CYCLOHEXANECARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(5-PHENYL-2-SUCCINYL-17(3-TERT-BUTOXYCARBONYLMETHYL-CARBAMOYL)-METHYL-

VIRO-6

PROPYL)-7,12-DIHYDROXY-10,13-DIMETHYL-HEXADECAHYDRO-CYCLOPENTA(A)PHENANTHREN-3-YLOYMETHOXYCARBONYL-THIOPHEN-3-YL)AMINO-PIPERIDINIUM CHLORIDE;

METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(5-PHENYL-2-SUCCINYL-17(3-CARBONYLMETHYL-CARBAMOYL)-METHYL-PROPYL)-7,12-DIHYDROXY-10, 13-DIMETHYL-HEXADECAHYDRO-CYCLOPENTA(A)PHENANTHREN-3-YLOYMETHOXYCARBONYL-THIOPHEN-3-YL)AMINO-PIPERIDINIUM CHLORIDE;

4-[(2-ETHOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(2-PHENOXY-CARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-AMINO]-PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-[2-(MORPHOLINE-4-CARBONYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-AMINO]-PIPERIDINIUM CHLORIDE;

4-[[2-[1-(2,2-DIMETHYL-PROPIONYLOXY)-2-METHYL-PROPOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-SEC-BUTOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(1-ISOPROPOXYCARBONYLOXY-2-METHYL-PROPOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-SEC-BUTOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-

VIRO-6

AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID TERT-BUTOXYCARBONYLAMINOACETOXYMETHYL ESTER;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2-TERT-BUTOXYCARBONYLAMINO-3-METHYL-BUTYRYLOXYMETHYL ESTER;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID AMINOACETOXYMETHYL ESTER, BIS TRIFLUOROACETATE SALT;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2-AMINO-3-METHYL-BUTYRYLOXYMETHYL ESTER, BIS TRIFLUOROACETATE SALT;

4-[[2-(1-ISOPROPOXYCARBONYLOXY-1-METHYL-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 1-(1-METHYL-CYCLOHEXANECARBONYLOXY)-ETHYL ESTER;

4-[[2-(1-TERT-BUTOXYCARBONYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-((4-METHYL-CYCLOHEXANECARBONYL)-{2-[1-(1-METHYL-CYCLOHEXANECARBONYLOXY)-ETHOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL}-AMINO)-PIPERIDINIUM;

PYRROLIDINE-1,2-DICARBOXYLIC ACID 1-TERT-BUTYL ESTER 2-{3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBONYLOXYMETHYL} ESTER;

4-METHYL-PIPERAZINE-1-CARBOXYLIC ACID 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBONYLOXYMETHYL ESTER DIHYDROCHLORIDE SALT;

VIRO-6

4-Methyl-piperazine-1-carboxylic acid-3-[(4-methyl-cyclohexanecarbonyl)-(1-methyl-piperidin-4-yl)-amino]-5-phenyl-thiophene-2-carbonyloxymethyl ester dihydrochloride salt;

4-[[2-(1-CYCLOHEXYLOXYCARBONYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

2-{3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBONYLOXYMETHOXYCARBONYL}-PYRROLIDINIUM; BIS-TRIFLUORO-ACETATE;

4-[[2-(1-ISOBUTYRYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID PYRIDIN-2-YL ESTER;

4-[[2-(1-ACETOXY-1-METHYL-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2-OXO-PYRROLIDIN-1-YLMETHYL ESTER;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(2-PHENOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-AMINO]-PIPERIDINIUM CHLORIDE;

1-METHYL-4-{(4-METHYL-CYCLOHEXANECARBONYL)-[5-PHENYL-2-(PYRIDIN-3-YLOXYCARBONYL)-THIOPHEN-3-YL]-AMINO}-PIPERIDINIUM; CHLORIDE;

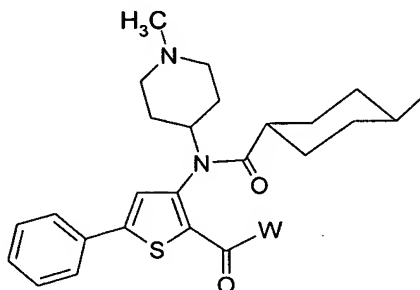
4-[[2-[1-(4-HYDROXY-5-HYDROXYMETHYL-TETRAHYDRO-FURAN-2-YL)-2-OXO-1,2-DIHYDRO-PYRIMIDIN-4-YLCARBAMOYL]-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

VIRO-6

4-[[2-(1-METHOXYCARBONYL-2-METHYL-PROPYLCARBAMOYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(1-METHOXYCARBONYL-ETHYLCARBAMOYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM;
and pharmaceutically acceptable salts thereof.

15. (Currently Amended): A pharmaceutical composition comprising at least one compound of formula I:

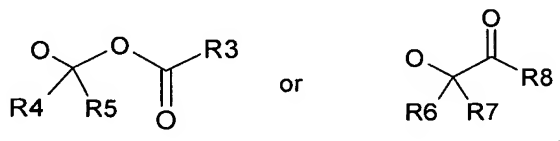


(I)

or a pharmaceutically acceptable salt thereof;

wherein [[:]]

W is C₁₋₁₂ alkyloxy, C₆₋₁₂ arylalkyloxy, amino acid ester, nucleoside, C₆₋₁₂ heteroaralkyloxy, C₆ aryloxy, 5-6 membered heteroaryloxy,



R₃ and R₈ are each independently C₁₋₁₂ alkyl, C₆₋₁₀ aryl, C₆₋₁₀ arylalkyl, C₃₋₁₀ heterocycle, C₃₋₁₂ heteroaralkyl, C₆₋₁₂ aralkyl, C₁₋₁₂ alkyloxy, C₆₋₁₀ aryloxy or NR₁₀R₁₁;

R₁₀ and R₁₁ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₂ aryl, C₃₋₁₀ heterocycle, C₆₋₁₂ aralkyl or C₃₋₁₀ heteroaralkyl;

VIRO-6

R₄ and R₅ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₀ aryl, -O(CO)C₁₋₆ alkyl or C₃₋₁₀ heterocycle; and

R₆ and R₇ are each independently ~~chosen from~~ H, C₁₋₁₂ alkyl, C₆₋₁₀ aryl, -O(CO)C₁₋₆ alkyl or C₃₋₁₀ heterocycle;

and at least one pharmaceutically acceptable carrier or excipient;

wherein

the above alkyl groups are each a straight chain or branched chain hydrocarbon moiety which optionally contain at least one unsaturated group and which is optionally substituted by one or more of halogen, nitro, nitroso, SO₃C₁₋₆ alkyl, SO₂C₁₋₆ alkyl, PO₃RcRd, amido, C₁₋₆ alkyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, amino, COOH, C(O)O-C₁₋₆ alkyl, cyano, azido, amidino or guanido;

Rc and Rd are each independently H or C₁₋₆ alkyl or Rc and Rd are taken together with the oxygen atoms to form a 5 to 10 membered heterocycle;

the above cycloalkyl groups are each a cyclic alkyl which optionally contain at least one unsaturated group;

the above alkyloxy are each an alkyl group as defined above which is covalently bonded to the adjacent atom through an oxygen atom;

the above amino groups are each optionally substituted by alkyl, aryl, or arylalkyl;

the above amido groups are each -CONH₂, CONH(isopropyl), CON(CH₃)₂;

the above aryl groups are each a carbocyclic moiety containing at least one benzenoid-type ring which is optionally substituted by one or more of halogen, nitro, nitroso, SO₃C₁₋₆ alkyl, SO₂C₁₋₆ alkyl, PO₃RcRd, amido, C₁₋₆ alkyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, amino, COOH, C(O)O-C₁₋₆ alkyl, cyano, azido, amidino or guanido;

the above aralkyl are each an aryl group attached to the adjacent atom by a C₁₋₆ alkyl, C₁₋₆ alkenyl, or C₁₋₆ alkynyl;

the above aralkyloxy groups are each an aralkyl group which is covalently bonded to the adjacent atom through an oxygen atom;

VIRO-6

the above amino acid ester groups are each an essential or non-essential alpha amino acid, beta amino acid or esterified amino acid carboxylate;

the above heterocycle groups are each a saturated or unsaturated, cyclic moiety wherein said cyclic moiety is interrupted by at least one heteroatom, selected from oxygen, sulfur and nitrogen, which is optionally substituted by halogen, nitro, nitroso, SO₃C₁₋₆ alkyl, SO₂C₁₋₆ alkyl, PO₃RcRd, amido, C₁₋₆ alkyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, amino, COOH, C(O)O-C₁₋₆ alkyl, cyano, azido, amidino or guanido; and

the above heteroaralkyl groups are each a heterocycle group attached to the adjacent atom by a C₁₋₆ alkyl, C₁₋₆ alkenyl, or C₁₋₆ alkynyl.

16. (Previously Presented): A pharmaceutical composition according to claim 15, further comprising at least one additional agent which is a viral serine protease inhibitor, viral polymerase inhibitor, viral helicase inhibitor, immunomodulating agent, antioxidant agent, antibacterial agent, therapeutic vaccine, hepatoprotectant agent or antisense agent.

17. (Original): A pharmaceutical composition of claim 16, wherein the additional agent is interferon α , ribavirin, silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine or cyclosporin.

18. (Currently Amended): A pharmaceutical composition comprising at least one compound selected from:

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2,2-DIMETHYL-PROPIONYLOXYMETHY;

4-[(2-ISOPROPOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

4-[(2-ISOPROPYLCARBAMOYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM

VIRO-6

CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-[2-(5-METHYL-2-OXO-[1,3]DIOXOL-4-YLMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-AMINO]-PIPERIDINIUM;

4-[[2-(1-ISOPROPOXYCARBONYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-[1-(2,2-DIMETHYL-PROPIONYLOXY)-ETHOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(ISOPROPOXYCARBONYLOXY-PHENYL-METHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(CYCLOHEXYLOXYCARBONYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-[(2,2-DIMETHYL-PROPIONYLOXY)-PHENYL-METHOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(5-PHENYL-2-PROPIONYLOXYMETHOXYCARBONYL-THIOPHEN-3-YL)-AMINO]-PIPERIDINIUM CHLORIDE;

4-[[2-(FURAN-2-CARBONYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-BENZOYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-CYCLOHEXANECARBONYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-

VIRO-6

PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(5-PHENYL-2-SUCCINYL-17(3-TERT-BUTOXYCARBONYLMETHYL-CARBAMOYL)-METHYL-PROPYL)-7,12-DIHYDROXY-10,13-DIMETHYL-HEXADECAHYDRO-CYCLOPENTA(A)PHENANTHREN-3-YLOY METHOXYCARBONYL-THIOPHEN-3-YL)AMINO-PIPERIDINIUM CHLORIDE;

METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(5-PHENYL-2-SUCCINYL-17(3-CARBONYLMETHYL-CARBAMOYL)-METHYL-PROPYL)-7,12-DIHYDROXY-10,13-DIMETHYL-HEXADECAHYDRO-CYCLOPENTA(A)PHENANTHREN-3-YLOY METHOXYCARBONYL-THIOPHEN-3-YL)AMINO-PIPERIDINIUM CHLORIDE;

4-[(2-ETHOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(2-PHENOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-AMINO]-PIPERIDINIUM CHLORIDE;

1-METHYL-4-{(4-METHYL-CYCLOHEXANECARBONYL)-[2-(MORPHOLINE-4-CARBONYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-AMINO}-PIPERIDINIUM CHLORIDE;

4-[(2-[(1-(2,2-DIMETHYL-PROPIONYLOXY)-2-METHYL-PROPOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL])-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-SEC-BUTOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-(1-ISOPROPOXYCARBONYLOXY-2-METHYL-PROPOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-SEC-BUTOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

VIRO-6

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID TERT-BUTOXYCARBONYLAMINOACETOXYMETHYL ESTER;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2-TERT-BUTOXYCARBONYLAMINO-3-METHYL-BUTYRYLOXYMETHYL ESTER;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID AMINOACETOXYMETHYL ESTER, BIS TRIFLUOROACETATE SALT;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2-AMINO-3-METHYL-BUTYRYLOXYMETHYL ESTER, BIS TRIFLUOROACETATE SALT;

4-[[2-(1-ISOPROPOXYCARBONYLOXY-1-METHYL-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 1-(1-METHYL-CYCLOHEXANECARBONYLOXY)-ETHYL ESTER;

4-[[2-(1-TERT-BUTOXYCARBONYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-((4-METHYL-CYCLOHEXANECARBONYL)-{2-[1-(1-METHYL-CYCLOHEXANECARBONYLOXY)-ETHOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL}-AMINO)-PIPERIDINIUM;

PYRROLIDINE-1,2-DICARBOXYLIC ACID 1-TERT-BUTYL ESTER 2-{3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBONYLOXYMETHYL} ESTER;

4-METHYL-PIPERAZINE-1-CARBOXYLIC ACID 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-

VIRO-6

THIOPHENE-2-CARBONYLOXYMETHYL ESTER DIHYDROCHLORIDE SALT;

4-Methyl-piperazine-1-carboxylic acid 3-[(4-methyl-cyclohexanecarbonyl)-(1-methyl-piperidin-4-yl)-amino]-5-phenyl-thiophene-2-carbonyloxymethyl ester dihydrochloride salt;

4-[[2-(1-CYCLOHEXYLOXYCARBONYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

2-{3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBONYLOXYMETHOXYCARBONYL}-PYRROLIDINIUM; BIS-TRIFLUORO-ACETATE;

4-[[2-(1-ISOBUTYRYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID PYRIDIN-2-YL ESTER;

4-[[2-(1-ACETOXY-1-METHYL-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2-OXO-PYRROLIDIN-1-YLMETHYL ESTER;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(2-PHENOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL)-AMINO]-PIPERIDINIUM CHLORIDE;

1-METHYL-4-{(4-METHYL-CYCLOHEXANECARBONYL)-[5-PHENYL-2-(PYRIDIN-3-YLOXYCARBONYL)-THIOPHEN-3-YL]-AMINO}-PIPERIDINIUM; CHLORIDE;

4-[[2-[1-(4-HYDROXY-5-HYDROXYMETHYL-TETRAHYDRO-FURAN-2-YL)-2-OXO-1,2-DIHYDRO-PYRIMIDIN-4-YLCARBAMOYL]-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(1-METHOXYCARBONYL-2-METHYL-PROPYLCARBAMOYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

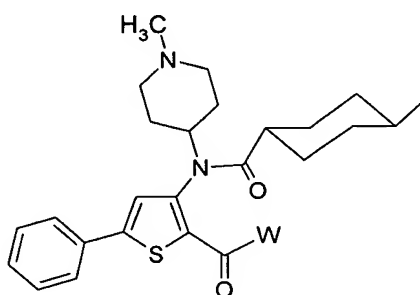
4-[[2-(1-METHOXYCARBONYL-ETHYLCARBAMOYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM;

VIRO-6

and pharmaceutically acceptable salts thereof;

and at least one pharmaceutically acceptable carrier or excipient.

19. (Currently Amended): A method for inhibiting or reducing the activity of viral polymerase in a host comprising administering to the host a therapeutically effective amount of at least one compound of formula I:

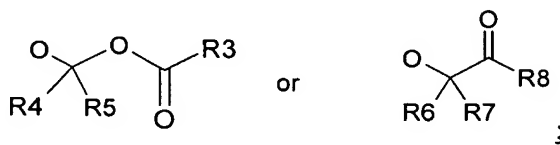


(I)

or a pharmaceutically acceptable salt thereof;

wherein [[:]]

W is C₁₋₁₂ alkyloxy, C₆₋₁₂ arylalkyloxy, amino acid ester, nucleoside, C₆₋₁₂ heteroarylalkyloxy, C₆ aryloxy, 5-6 membered heteroaryloxy,



R₃ and R₈ are each independently C₁₋₁₂ alkyl, C₆₋₁₀ aryl, C₆₋₁₀ arylalkyl, C₃₋₁₀ heterocycle, C₃₋₁₂ heteroarylalkyl, C₆₋₁₂ aralkyl, C₁₋₁₂ alkyloxy, C₆₋₁₀ aryloxy or NR₁₀R₁₁;

R₁₀ and R₁₁ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₂ aryl, C₃₋₁₀ heterocycle, C₆₋₁₂ aralkyl or C₃₋₁₀ heteroarylalkyl;

R₄ and R₅ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₀ aryl, -O(CO)C₁₋₆ alkyl or C₃₋₁₀

VIRO-6

heterocycle; and

R₆ and R₇ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₀ aryl, -O(CO)C₁₋₆ alkyl or C₃₋₁₀ heterocycle; and

at least one pharmaceutically acceptable carrier or excipient;

wherein

the above alkyl groups are each a straight chain or branched chain hydrocarbon moiety which optionally contain at least one unsaturated group and which is optionally substituted by one or more of halogen, nitro, nitroso, SO₃C₁₋₆ alkyl, SO₂C₁₋₆ alkyl, PO₃RcRd, amido, C₁₋₆ alkyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, amino, COOH, C(O)O-C₁₋₆ alkyl, cyano, azido, amidino or guanido;

Rc and Rd are each independently H or C₁₋₆ alkyl or Rc and Rd are taken together with the oxygen atoms to form a 5 to 10 membered heterocycle;

the above cycloalkyl groups are each a cyclic alkyl which optionally contain at least one unsaturated group;

the above alkyloxy are each an alkyl group as defined above which is covalently bonded to the adjacent atom through an oxygen atom;

the above amino groups are each optionally substituted by alkyl, aryl, or arylalkyl;

the above amido groups are each -CONH₂, CONH(isopropyl), CON(CH₃)₂;

the above aryl groups are each a carbocyclic moiety containing at least one benzenoid-type ring which is optionally substituted by one or more of halogen, nitro, nitroso, SO₃C₁₋₆ alkyl, SO₂C₁₋₆ alkyl, PO₃RcRd, amido, C₁₋₆ alkyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, amino, COOH, C(O)O-C₁₋₆ alkyl, cyano, azido, amidino or guanido;

the above aralkyl are each an aryl group attached to the adjacent atom by a C₁₋₆ alkyl, C₁₋₆ alkenyl, or C₁₋₆ alkynyl;

the above aralkyloxy groups are each an aralkyl group which is covalently bonded to the adjacent atom through an oxygen atom;

the above amino acid ester groups are each an essential or non-essential alpha amino acid,

VIRO-6

beta amino acid or esterified amino acid carboxylate;

the above heterocycle groups are each a saturated or unsaturated, cyclic moiety wherein said cyclic moiety is interrupted by at least one heteroatom, selected from oxygen, sulfur and nitrogen, which is optionally substituted by halogen, nitro, nitroso, SO₃C₁₋₆ alkyl, SO₂C₁₋₆ alkyl, PO₃RcRd, amido, C₁₋₆ alkyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, amino, COOH, C(O)O-C₁₋₆ alkyl, cyano, azido, amidino or guanido; and

the above heteroaralkyl groups are each a heterocycle group attached to the adjacent atom by a C₁₋₆ alkyl, C₁₋₆ alkenyl, or C₁₋₆ alkynyl.

20. (Original): A method of claim 19, wherein viral polymerase is a Flaviviridae viral polymerase.

21. (Currently Amended): A method for inhibiting or reducing the activity of viral polymerase in a host comprising administering a therapeutically effective amount of at least one compound selected from:

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2,2-DIMETHYL-PROPIONYLOXYMETHY;

4-[(2-ISOPROPOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

4-[(2-ISOPROPYLCARBAMOYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-{(4-METHYL-CYCLOHEXANECARBONYL)-[2-(5-METHYL-2-OXO-[1,3]DIOXOL-4-YLMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-AMINO}-PIPERIDINIUM;

4-[[2-(1-ISOPROPOXYCARBONYLOXY-ETHOXYCARBONYL)-5-PHENYL-

VIRO-6

THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-[1-(2,2-DIMETHYL-PROPIONYLOXY)-ETHOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(ISOPROPOXYCARBONYLOXY-PHENYL-METHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(CYCLOHEXYLOXYCARBONYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-[(2,2-DIMETHYL-PROPIONYLOXY)-PHENYL-METHOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(5-PHENYL-2-PROPIONYLOXYMETHOXYCARBONYL-THIOPHEN-3-YL)-AMINO]-PIPERIDINIUM CHLORIDE;

4-[[2-(FURAN-2-CARBONYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(BENZOYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(CYCLOHEXANECARBONYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(5-PHENYL-2-SUCCINYL-17(3-TERT-BUTOXYCARBONYLMETHYL-CARBAMOYL)-METHYL-PROPYL)-7,12-DIHYDROXY-10,13-DIMETHYL-HEXADECAHYDRO-CYCLOPENTA(A)PHENANTHREN-3-YLOXYMETHOXYCARBONYL-THIOPHEN-3-

VIRO-6

YL)AMINO-PIPERIDINIUM CHLORIDE;

METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(5-PHENYL-2-SUCCINYLMETHYL-17(3-CARBONYLMETHYL-CARBAMOYL)-METHYL-PROPYL)-7,12-DIHYDROXY-10, 13-DIMETHYL-HEXADECALYDRO-CYCLOPENTA(A)PHENANTHREN-3-YLOXYMETHOXY-CARBONYL-THIOPHEN-3-YL)AMINO-PIPERIDINIUM CHLORIDE;

4-[(2-ETHOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(2-PHENOXY-CARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-AMINO]-PIPERIDINIUM CHLORIDE;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-[2-(MORPHOLINE-4-CARBONYLOXYMETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-AMINO]-PIPERIDINIUM CHLORIDE;

4-[[2-[1-(2,2-DIMETHYL-PROPYNYLOXY)-2-METHYL-PROPOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-SEC-BUTOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(1-ISOPROPOXYCARBONYLOXY-2-METHYL-PROPOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[(2-SEC-BUTOXYCARBONYLOXYMETHOXYCARBONYL-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHEN-2-CARBOXYLIC ACID TERT-BUTOXYCARBONYLAMINOACETOXYMETHYL ESTER;

VIRO-6

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2-TERT-BUTOXYCARBONYLAMINO-3-METHYL-BUTYRYLOXYMETHYL ESTER;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID AMINOACETOXYMETHYL ESTER, BIS TRIFLUOROACETATE SALT;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2-AMINO-3-METHYL-BUTYRYLOXYMETHYL ESTER, BIS TRIFLUOROACETATE SALT;

4-[[2-(1-ISOPROPOXYCARBONYLOXY-1-METHYL-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 1-(1-METHYL-CYCLOHEXANECARBONYLOXY)-ETHYL ESTER;

4-[[2-(1-TERT-BUTOXYCARBONYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

1-METHYL-4-((4-METHYL-CYCLOHEXANECARBONYL)-{2-[1-(1-METHYL-CYCLOHEXANECARBONYLOXY)-ETHOXYCARBONYL]-5-PHENYL-THIOPHEN-3-YL}-AMINO)-PIPERIDINIUM;

PYRROLIDINE-1,2-DICARBOXYLIC ACID 1-TERT-BUTYL ESTER 2-{3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBONYLOXYMETHYL} ESTER;

4-METHYL-PIPERAZINE-1-CARBOXYLIC ACID 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBONYLOXYMETHYL ESTER DIHYDROCHLORIDE SALT;

~~4-Methyl-piperazine-1-carboxylic acid 3-[(4-methyl-cyclohexanecarbonyl)-(1-methyl-piperidin-4-yl)-amino]-5-phenyl-thiophene-2-carbonyloxymethyl ester dihydrochloride salt;~~

VIRO-6

4-[[2-(1-CYCLOHEXYLOXYCARBONYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

2-{3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBONYLOXYMETHOXYCARBONYL}-PYRROLIDINIUM; BIS-TRIFLUORO-ACETATE;

4-[[2-(1-ISOBUTYRYLOXY-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM; CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID PYRIDIN-2-YL ESTER;

4-[[2-(1-ACETOXY-1-METHYL-ETHOXYCARBONYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 2-OXO-PYRROLIDIN-1-YLMETHYL ESTER;

1-METHYL-4-[(4-METHYL-CYCLOHEXANECARBONYL)-(2-PHENOXY-CARBONYL-5-PHENYL-THIOPHEN-3-YL)-AMINO]-PIPERIDINIUM CHLORIDE;

1-METHYL-4-{(4-METHYL-CYCLOHEXANECARBONYL)-[5-PHENYL-2-(PYRIDIN-3-YLOXYCARBONYL)-THIOPHEN-3-YL]-AMINO}-PIPERIDINIUM; CHLORIDE;

4-[[2-[1-(4-HYDROXY-5-HYDROXYMETHYL-TETRAHYDRO-FURAN-2-YL)-2-OXO-1,2-DIHYDRO-PYRIMIDIN-4-YLCARBAMOYL]-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

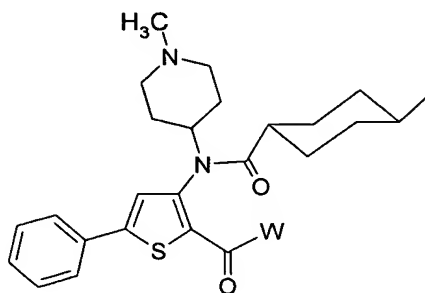
4-[[2-(1-METHOXYCARBONYL-2-METHYL-PROPYLCARBAMOYL)-5-PHENYL-THIOPHEN-3-YL]-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM CHLORIDE;

4-[[2-(1-METHOXYCARBONYL-ETHYLCARBAMOYL)-5-PHENYL-THIOPHEN-3-

VIRO-6

YLJ-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-1-METHYL-PIPERIDINIUM;
and pharmaceutically acceptable salts thereof.

22. (Currently Amended): A combination comprising a least one compound of formula I:

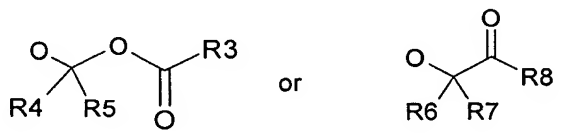


(I)

or a pharmaceutically acceptable salt thereof;

wherein [[:]]

W is C₁₋₁₂ alkyloxy, C₆₋₁₂ arylalkyloxy, amino acid ester, nucleoside, C₆₋₁₂ heteroaralkyloxy, C₆ aryloxy, 5-6 membered heteroaryloxy,



R₃ and R₈ are each independently C₁₋₁₂ alkyl, C₆₋₁₀ aryl, C₆₋₁₀ arylalkyl, C₃₋₁₀ heterocycle, C₃₋₁₂ heteroaralkyl, C₆₋₁₂ aralkyl, C₁₋₁₂ alkyloxy, C₆₋₁₀ aryloxy or NR₁₀R₁₁;

R₁₀ and R₁₁ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₂ aryl, C₃₋₁₀ heterocycle, C₆₋₁₂ aralkyl or C₃₋₁₀ heteroaralkyl;

R₄ and R₅ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₀ aryl, -O(CO)C₁₋₆ alkyl or C₃₋₁₀ heterocycle; and

R₆ and R₇ are each independently H, C₁₋₁₂ alkyl, C₆₋₁₀ aryl, -O(CO)C₁₋₆ alkyl or C₃₋₁₀ heterocycle;

VIRO-6

and one or more additional agent which is a viral serine protease inhibitor, viral polymerase inhibitor and viral helicase inhibitor, immunomodulating agent, antioxidant agent, antibacterial agent, therapeutic vaccine, hepatoprotectant agent or antisense agent;

wherein

the above alkyl groups are each a straight chain or branched chain hydrocarbon moiety which optionally contain at least one unsaturated group and which is optionally substituted by one or more of halogen, nitro, nitroso, $\text{SO}_3\text{C}_{1-6}$ alkyl, $\text{SO}_2\text{C}_{1-6}$ alkyl, PO_3RcRd , amido, C_{1-6} alkyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{6-12} aryloxy, $\text{C}(\text{O})\text{C}_{1-6}$ alkyl, $\text{C}(\text{O})\text{C}_{6-12}$ aryl, $\text{C}(\text{O})\text{C}_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, amino, COOH , $\text{C}(\text{O})\text{O}-\text{C}_{1-6}$ alkyl, cyano, azido, amidino or guanido;

Rc and Rd are each independently H or C_{1-6} alkyl or Rc and Rd are taken together with the oxygen atoms to form a 5 to 10 membered heterocycle;

the above cycloalkyl groups are each a cyclic alkyl which optionally contain at least one unsaturated group;

the above alkyloxy are each an alkyl group as defined above which is covalently bonded to the adjacent atom through an oxygen atom;

the above amino groups are each optionally substituted by alkyl, aryl, or arylalkyl;

the above amido groups are each $-\text{CONH}_2$, $\text{CONH}(\text{isopropyl})$, $\text{CON}(\text{CH}_3)_2$;

the above aryl groups are each a carbocyclic moiety containing at least one benzenoid-type ring which is optionally substituted by one or more of halogen, nitro, nitroso, $\text{SO}_3\text{C}_{1-6}$ alkyl, $\text{SO}_2\text{C}_{1-6}$ alkyl, PO_3RcRd , amido, C_{1-6} alkyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{6-12} aryloxy, $\text{C}(\text{O})\text{C}_{1-6}$ alkyl, $\text{C}(\text{O})\text{C}_{6-12}$ aryl, $\text{C}(\text{O})\text{C}_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, amino, COOH , $\text{C}(\text{O})\text{O}-\text{C}_{1-6}$ alkyl, cyano, azido, amidino or guanido;

the above aralkyl are each an aryl group attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl;

the above aralkyloxy groups are each an aralkyl group which is covalently bonded to the adjacent atom through an oxygen atom;

the above amino acid ester groups are each an essential or non-essential alpha amino acid, beta amino acid or esterified amino acid carboxylate;

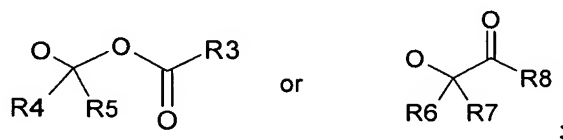
VIRO-6

the above heterocycle groups are each a saturated or unsaturated, cyclic moiety wherein said cyclic moiety is interrupted by at least one heteroatom, selected from oxygen, sulfur and nitrogen, which is optionally substituted by halogen, nitro, nitroso, $\text{SO}_3\text{C}_{1-6}$ alkyl, $\text{SO}_2\text{C}_{1-6}$ alkyl, PO_3RcRd , amido, C_{1-6} alkyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{6-12} aryloxy, $\text{C}(\text{O})\text{C}_{1-6}$ alkyl, $\text{C}(\text{O})\text{C}_{6-12}$ aryl, $\text{C}(\text{O})\text{C}_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, amino, COOH , $\text{C}(\text{O})\text{O}-\text{C}_{1-6}$ alkyl, cyano, azido, amidino or guanido; and

the above heteroaralkyl groups are each a heterocycle group attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl.

23. (Previously Presented): A compound according to claim 1, wherein:

W is



R_3 or R_8 are each methyl, fluoromethyl, difluoromethyl, trifluoromethyl, ethyl, fluoroethyl, difluoroethyl, trifluoroethyl, propyl, isopropyl, cyclopropyl, butyl, isobutyl, t-butyl, pentyl, cyclopentyl, hexyl, cyclohexyl, methoxy, ethyloxy, propyloxy, isopropyloxy, cyclopropyloxy, t-butyloxy, phenyl, phenoxy, thienyl, furanyl, pyridyl, oxazolyl, thiazolyl, pyrrolyl, benzofuranyl, indolyl, benzoxazolyl, benzothienyl, benzothiazolyl, quinoliny, pyridinyl, thiophenyl, benzofuran, thiazolyl, pyrazolyl, pyridinyl, isoxazolyl or tetrazolyl;

R_4 is H, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, ethyl, fluoroethyl, difluoroethyl, trifluoroethyl, propyl, isopropyl, cyclopropyl, butyl, isobutyl, t-butyl, pentyl, cyclopentyl, hexyl, cyclohexyl, or phenyl;

R_5 is H;

R_6 is H, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, ethyl, fluoroethyl, difluoroethyl, trifluoroethyl, propyl, isopropyl, cyclopropyl, butyl, isobutyl, t-butyl, pentyl, cyclopentyl, hexyl or cyclohexyl; and

R_7 is H.

VIRO-6